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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/828,474

04/20/2004

Tianmin Zhu

AM101007

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25291

7590

03/17/2009

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EXAMINER

PACKARD, BENJAMIN J

ART UNIT

PAPER NUMBER

1612

MAIL DATE

DELIVERY MODE

03/17/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/828,474	<b>Applicant(s)</b> ZHU ET AL.	
	<b>Examiner</b> Benjamin Packard	<b>Art Unit</b> 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 December 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-96 is/are pending in the application.
- 4a) Of the above claim(s) 9-67 and 74-96 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 68-73 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1pg (12/17/08)</u>  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicants' arguments, filed 12/17/08, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

#### ***Claim Rejections - 35 USC § 103***

**Claims 1-8 and 68-73** stand rejected under 35 U.S.C. 103(a) as being unpatentable over Creemer et al (5,480,906, see IDS dated 4/20/2004) in view of Gutman et al (Toxins and Signal Transduction, Published by CRC Press, 1997, pg 429) and Zhu et al (US 6,331,547).

Applicants assert: (1) The art is unpredictable, where Applicants cited Greenwald (J. controlled Release, IDS dated 12/17/08) as teaching no low molecular weight small molecule drug conjugates have led to a clinically approved product. (2) The solubility of the compound in Zhu et al is different than wortmannin, thus removing motivation to increase water solubility. (3) The compound (j) of Creemer differs from the instantly claimed compound at position 17 and position 11, further that Zhu teaches derivatives of rapamycin. (4) Wortmannin and Rapamycin are different compounds. (5) It would not be obvious to PEGulate all known water insoluble compounds.

The Examiner disagrees. First, the unpredictable art argument appears to be directed to the method claims 3-8 where the composition claims do not require an active step of administration. Greenwald, while casting doubt on the predictability of treatment,

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does not teach away from using low molecular weight PEG prodrugs. After the discussion of a single experiment, Greenwald simply states "This example clearly illustrates the necessity for in vivo testing to verify in vitro cytotoxicity results." (pg 161) Such a statement suggests treatment may be reasonably expected when such results are found. The verification would then be an obvious testing step before administration.

Second, the differences in the specific solubility of the individual compounds are not at issue. Instead, it is the teaching of how to overcome a problem, i.e. limited solubility. Therefore, where wortmannin is taught to have limited solubility, it would be obvious to apply techniques for overcoming solubility issues of other compounds which have the same problem.

Third, the closest compound to Applicants formula III is not compound (j), but actually the disclosure of wormannin at col 1 lines 10-30, which differs only in the substituent of carbon 17. Creemer then teaches the modification of carbon 11 and 17, but did not specifically teach the instantly claimed substituent at carbon 17. Zhu et al taught the prodrug form which is then attached to carbon 17 to solve the solubility issue discussed above.

Fourth, Examiner acknowledges wortmannin and Rapamycin are distinct compounds, but the compound Rapamycin is not cited as part of the rejection. Instead, the Rapamycin-conjugate was cited for the teaching of using a conjugate to overcome water solubility issues. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091,

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231 USPQ 375 (Fed. Cir. 1986). Instead, the references are to be examined together for what is fairly suggested or taught by the combination, taken as a whole.

Fifth, Examiner is not citing an infinite number of compounds and possibilities, instead looking to one compound, wortmannin, and one conjugate, as disclosed by Zhu. Looking to the teaching of Zhu, one of ordinary skill would reasonably expect the conjugate portion of the compound disclosed in Zhu to increase solubility of other compounds with the same problem, such as disclosed in Creemer where the problem of solubility is taught by Gutman.

### ***Conclusion***

No claims allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-R 8-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/  
Examiner, Art Unit 1612

/Frederick Krass/  
Supervisory Patent Examiner, Art Unit 1612